saccharides having a degree of glucose polymerization of at least 3;

(2) Molecular weight

About 69,000-79,000 daltons on sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE);

(3) Isoelectric point (pI)

About 5.4-6.4 on isoelectrophoresis;

(4) Thermostability

Substantially not inactivated even when incubated in an aqueous solution (pH 7.0) at 85°C for 60 min.; and

(5) Amino acid sequence

An amino acid sequence which is not identical to SEQ ID NO:1 but which has physicochemical properties of (1) to (4) inherent to a thermostable enzyme of SEQ ID NO:1, said amino acid sequence comprising the sequence of at least two contiguous amino acid residues in SEQ ID NO:3 and/or SEQ ID NO:4.

REMARKS

The Office Action has been carefully reviewed. No claim is allowed. Claim 1 presently appears in this application and defines patentable subject matter warranting its allowance. Reconsideration and allowance are hereby respectfully solicited.

Claim 1 has been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 5,976,856. This rejection is now obviated by the terminal disclaimer attached hereto.

Claim 1 has been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Applicants have now amended claim 1, last line, to recite "and/or" and thereby making clear that at least two contiguous amino acid residues from SEQ ID NO:3 and/or SEQ ID NO:4 are present in the amino acid sequence of the purified recombinant thermostable enzyme. Accordingly, applicants believe that this rejection is overcome by the amendment to claim 1.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claim 1 has been rejected under 35 U.S.C. 112, first paragraph, because the examiner indicates that the specification, while being enabling for the enzyme of SEQ ID NO:1 or enzymes encoded by genes which will hybridize to SEQ ID NO:2 under specific conditions, does not reasonably provide enablement for any enzyme with the claimed properties.

It is said that applicants argue that the defined properties allow the skilled artisan to readily find other such enzymes by screening other microorganisms for those with the recited activity and further screening those with activity for the other recited characteristics. In response, the examiner states that it should be noted that the specification does not

teach an assay for the activity recited in part (1) of the claim which would be easy to use for screening large numbers of organisms. The examiner holds that the activity assay on pages 13-14 of the specification requires an HPLC separation of the products of the reaction which is difficult to use for large scale screening. It is further said by the examiner that, while the number of naturally occurring enzymes which meet all of these claimed properties (activity, molecular weight, pI, and thermos/ability) may not be enormous (although it could be a fairly substantial number as it is certainly not uncommon for enzymes with related activities to be similar in other properties as well as to be often evolutionarily related to each other), applicants claims are not limited to naturally occurring enzymes but also include all non-naturally occurring variants and fragments of such naturally occurring enzymes which retain the claimed physicochemical properties.

Furthermore, the examiner holds that, while the skilled artisan could readily make variants of the enzyme of SEQ ID NO:1 by using known mutagenesis techniques, such techniques would be sufficient for one of ordinary skill in the art to make and use variants with only a few substitutions by making several variants and testing for those which retain the claimed properties. The examiner asserts that such experimentation would be undue for those polypeptides with greater numbers of substitutions as the likelihood of a variant sequence retaining the claimed properties of the native polypeptide decreases substantially with each additional mutation while the number of possible variants which

could be made increases exponentially. It is the examiner's position that the claimed variants (i.e., those which retain the claimed physicochemical properties of the native polypeptide) with larger numbers of mutations are a very minute fraction of the possible variants which could be made and the experimentation required to make and test all the possibilities would be undue. This rejection is respectfully traversed.

Applicant believes that a purified recombinant thermostable enzyme of claim 1 is defined by the physicochemical properties (1) to (5) recited in the amended claim 1. In other words, an enzyme of claim 1 is defined by its action, molecular weight, isoelectric point and thermostability as well as its amino acid sequence. As disclosed in the specification at pages 21-22, Experiment 3-2, amino acid sequences of SEQ ID NO:3 and SEQ ID NO:4, which are partial amino acid sequences of SEQ ID NO:1, are very important for characterizing the enzyme of the present invention. Therefore, applicants submit that it is easily understood that the recitation of an amino acid sequence which is not identical to SEQ ID NO:1 but comprises "at least two contiguous amino acids in SEQ ID NO:3 and/or SEQ ID NO:4" is clear and well defines the claimed enzyme. Applicants again emphasize that the claimed enzyme is not defined with its amino acid sequence only, but defined with its (1) to (5) physicochemical properties.

Regarding the examiner's assertion that "the activity assay of pages 13-14 requires an HPLC separation of the products

of the reaction which is difficult to use for large scale screening", applicants respectfully disagree. It should be noted that HPLC at pages 13-14 of the specification is used not to screen the enzyme but to find out the substrate specificity" of the enzyme. As described there, the enzyme is used to act on various saccharides and the compositions of the products of the reaction are investigated by HPLC separation to determine the "substrate specificity" of the enzyme. Furthermore, contrary to the examiner's assertion that the specification does not teach an assay for the activity recited in part (1) of the claim which would be easy to use for screening large numbers of organisms, it is respectfully pointed out that the specification at page 12, last paragraph, provides an assay that can be used for such a purpose.

According to the disclosure of the specification and the properties (1) to (5) recited in amended claim 1, applicants believe that the screening of the enzyme can be readily conducted by a skilled artisan even if there are large numbers of specimen to be screened. For example, as the claimed enzyme has the property of thermostability as recited in property (4) in claim 1, a skilled artisan would first incubate the specimen in an aqueous solution (pH 7.0) at 85°C for 60 min. With this treatment, any enzymes which are not as stable as the claimed enzyme would lose their activity and would therefore be eliminated from consideration. The enzymatic activity of the specimens are then assayed by the method as disclosed at page 12,

third paragraph of the specification. Enzymes which retain their activity are those which have an amino acid sequence of SEQ ID NO:1 or an amino acid sequence as defined in property (5) of claim 1.

The above-mentioned operations are merely routine experimentation on the part of a skilled artisan and therefore the screening of the claimed enzyme does not require any undue experimentation. It is believed by applicants that the specification provides enablement for the claimed enzyme.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

In view of the above applicants submit that the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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"VERSION WITH MARKINGS TO SHOW CHANGES MADE"

IN THE CLAIMS

Claim 1 has been amended as follows:

1(Twice-amended). A purified recombinant thermostable enzyme having the following physicochemical properties:

(1) Action

Forming non-reducing saccharides having a trehalose structure as an end unit and having a degree of glucose polymerization of at least 3 from maltotetraose or reducing amylaceous saccharides having a degree of glucose polymerization of at least 3;

(2) Molecular weight

About 69,000-79,000 daltons on sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE);

(3) Isoelectric point (pI)

About 5.4-6.4 on isoelectrophoresis;

(4) Thermostability

Substantially not inactivated even when incubated in an aqueous solution (pH 7.0) at 85°C for 60 min.; and

(5) Amino acid sequence

An amino acid sequence which is not identical to SEQ ID NO:1 but which has physicochemical properties of (1) to (4) inherent to a

thermostable enzyme of SEQ ID NO:1, said amino acid sequence comprising the sequence of ~~one or more fragments of~~ at least two contiguous amino acid residues in SEQ ID NO:3 and/or SEQ ID NO:4.

claim of the above-identified application is obvious over any claim of Patent No. 5,976,856.

Respectfully submitted,

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